Remarks

I. Status

Claims 28-29, 31, 32, 36 and 52-81 are currently pending. All rejections based upon 35 U.S.C. §112 have been withdrawn in light of Applicants' prior amendments and remarks. All rejections based on prior art, with the exception of rejections made pursuant to the judicially created doctrine of obviousness-type double patenting have also been withdrawn.

II. The Information Disclosure Statement Form 1449

Applicants regret any inconvenience to the Examiner regarding the issue of consideration of references that have been previously submitted to the Examiner. A review of Applicants' files has revealed that the references provided in Applicants Information Disclosure Statement of November 27, 2000, were in fact considered by the Examiner as indicated by the initialing and return of Form 1449 with the Official Action of February 14, 2001.

III. The Rejections Pursuant to the Judicially Created Doctrine Of Obviousness-Type Double Patenting in light of U.S. Patent No. 6,184,344

Claims 28-29, 31, 32, 36 and 52-81 have been rejected pursuant to the judicially created doctrine of obviousness-type double patenting in light of U.S. Patent No. 6,184,344 in combination with the publication: Canne *et al.* JACS 117:2998-3007 (1995) ("Canne *et al.*"). Claims 32, 36 and 62-70 have been rejected pursuant to the judicially created doctrine of obviousness-type double patenting in light of commonly assigned U.S. Patent No. 6,184,344 in combination with Canne *et al.*, and Pavia *et al.* (Biorg. Medicinal Chem. Lett. 3:387-396) ("Pavia *et al.*"). U.S. Patent No. 6,184,344 is not commonly owned with the present application, but concerns an invention of Dr. Stephen Kent, who is one of the inventors of the present invention.

Applicants respectfully traverse the rejection and request reconsideration. Applicants submit that the essence of an obviousness-type double patenting rejection is that the presented claims are not patentably distinct from the ***claims*** of the prior-issued patent. Thus, it is respectfully submitted that only the content of the claims, and not the content of the ***specification*** of a patent is relevant to a double-patenting rejection. As such, Applicants submit that the alleged teachings of the patent, its figures and its Examples – all cited by the Examiner as a basis for the rejection – is in fact not a proper basis for a double patenting rejection.

For the convenience of the Examiner, Applicants have recited below claims 1-7 of U.S. Patent No. 6,184,344:

1. A method for ligating a first oligopeptide with a second oligopeptide end to end for producing an oligopeptide product, the method comprising the following steps:
Step A: admixing the first and second oligopeptides in a reaction solution including a catalytic thiol, the first oligopeptide including a C-terminal thioester, the second oligopeptide including an N-terminal cysteine having an unoxidized sulfhydryl side chain; then
Step B: condensing the unoxidized sulfhydryl side chain of the N-terminal cysteine with the C-terminal thioester for producing an intermediate oligopeptide linking the first and second oligopeptides with a β-aminothioester bond; and then
Step C: rearranging the β-aminothioester bond of the intermedite oligopeptide of said Step B for producing the oligopeptide product linking the first and second oligopeptides with an amide bond.

2. A method as described in claim 1 wherein, in said step A, the catalytic thiol is selected from the group consisting of unconjugated mercaptans and conjugated thiols.

3. A method as described in claim 2 wherein, in said step A, the catalytic thiol is benzyl mercaptan.

4. A method as described in claim 2 wherein, in said step A, the catalytic thiol is a conjugated thiol selected from the group consisting of thiophenol, 1-thio-2-nitrophenol, 2-thio-benzoic acid, 2-thio-pyridine, 4-thio-2-pyridinecarboxylic acid, and 4-thio-2-nitro-pyridine.

5. A method as described in claim 4 wherein, in said step A, the conjugated thiol is thiophenol.

6. An oligopeptide intermediate comprising:
a first oligopeptide segment having a C-terminal thioester,
a second oligopeptide segment having a N-terminal cysteine, and
a β-aminothioester linkage unit linking the C-terminal thioester and the N-terminal cysteine, said β-aminothioester linkage unit spontaneously rearranging intramolecularly to form an amide bond linking said first and second oligopeptides segments end to end.

7. A method for producing an oligopeptide having a C-terminal thioester, the method comprising the following steps:
Step A: providing a resin having a linker with an unoxidized thiol;
Step B: providing a Boc-amino acid succinimide ester; then
Step C: admixing the resin of said Step A and the Boc-amino acid succinimide ester of said Step B under reaction conditions for producing a Boc-amino thioester-resin; then
Step D: assembling an oligopeptide onto the Boc-amino thioester-resin by stepwise solid phase peptide synthesis; then
Step E: cleaving the Boc-amino thioester-resin of said Step D with HF for producing an oligopeptide having a C-terminal thiol; and then
Step F: converting the oligopeptide having a C-terminal thiol of said Step E to the oligopeptide having a C-terminal thioester.

In contrast to such claims, the present invention is directed to a method of producing a "cross-over" ***chemokine*** protein having at least one peptide segment whose sequence is derived from a first chemokine protein, and which comprises a functional protein module of such first chemokine protein and at least one peptide segment whose sequence is derived from a second chemokine protein and which comprises a functional protein module of such first chemokine protein. It is respectfully submitted that the mere disclosure of the claims of the '344 Patent of a method for ligating together two oligonucleotides does not render obvious the selection of functional ***chemokine*** protein modules or the production of a hybrid ("cross-over") ***chemokine***. There is simply no suggestion or motivation in the claims of the '344 Patent to make such the selection being presently claimed or to produce the result recited in the present claims.

Applicants respectfully submit that the secondary references cited by the Examiner, Canne *et al.* and Pavia *et al.* fail to remedy this deficiency. Indeed, as admitted by the Examiner, the cited Canne *et al.* reference fails to disclose or suggest the ligation of peptide segments of chemokines, and as such fails to suggest a modification of the invention claimed in the '344 Patent in which chemokine peptide segments are employed. Moreover, as discussed previously, the cited Canne *et al.* reference teaches the ***C-terminal to C-terminal ligation*** of two peptide domains (see page 2999, first sentence of paragraph bridging left and right columns) and as such fails to suggest a modification of the invention claimed in the '344 Patent in which peptide segments are joined in an ***N-terminal to C-terminal*** manner (as presently claimed). It is respectfully submitted that the Examiner's concern that the citing of the Dawson *et al.* publication in the cited Canne *et al.* reference would not alter this conclusion in the absence of hindsight.

The failure of the cited Canne *et al.* reference to remedy the deficiency in the rejection is not remedied by the cited Pavia *et al.* reference. Significantly, as previously discussed, none of the multiple synthetic approaches discussed in the Pavia *et al.* reference concerns the joining, by any means or in any orientation, of peptide domains of different proteins to form a library of cross-over proteins. Applicants again respectfully submit that the cited Pavia *et al.* reference provides no more than a general review of combinatorial chemistry methods unrelated to those of the present invention. As such, the reference, alone or in combination with the cited Canne *et al.* reference, is insufficient to support a double patenting rejection of the present claims in light of the claims of the '344 Patent.

Applicants accordingly submit that the rejections of claims 28-29, 31, 32, 36 and 52-81, and of 32, 36 and 62-70 pursuant to the judicially created doctrine of obviousness-type double patenting in light of U.S. Patent No. 6,184,344 in combination with Canne *et al.* or Canne *et al.* and Pavia *et al.* may be properly withdrawn.

IV. The Rejections Pursuant to the Judicially Created Doctrine Of Obviousness-Type Double Patenting in light of U.S. Patent No. 6,326,468

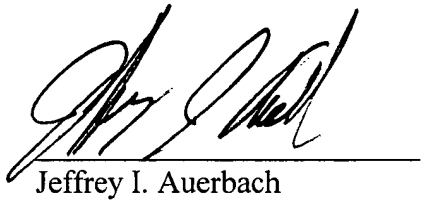
Claims 28-29, 31, 36 and 52-81 have been rejected pursuant to the judicially created doctrine of obviousness-type double patenting in light of U.S. Patent No. 6,326,468 in combination with the publication: Canne *et al.* JACS 117:2998-3007 (1995) ("Canne *et al.*"). U.S. Patent No. 6,326,468 is commonly owned with the present application.

In response to such rejection, Applicants respectfully submit the enclosed Terminal Disclaimer, which terminally disclaims such portion of the patent that will issue on the present application that would exceed the term of U.S. Patent No. 6,326,468 and respectfully submit that such action fully responds to the concerns of the Examiner. Accordingly, Applicants respectfully submit that the rejections based on the judicially created doctrine of obviousness-type double patenting may now be properly withdrawn.

IV. Concluding Remarks

Having now fully responded to all outstanding rejections, Applicants respectfully submit that the present application is in condition for Allowance, and earnestly solicit early notice of such favorable action. The Examiner is respectfully invited to contact the undersigned with respect to any issues regarding this application.

Respectfully Submitted,



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